Connecting via Winsock to STN

```
Welcome to STN International! Enter x:x
```

LOGINID:ssspta1202txn

specific topic.

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
* * * * * * * *
                     Welcome to STN International
                 Web Page URLs for STN Seminar Schedule - N. America
NEWS 1
                 "Ask CAS" for self-help around the clock
NEWS 2
NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks
                 (ROSPATENT) added to list of core patent offices covered
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status
                 data from INPADOC
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enhanced
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new
NEWS 15 APR 04 EMBASE - Database reloaded and enhanced
NEWS 16 APR 18 New CAS Information Use Policies available online
NEWS 17 APR 25 Patent searching, including current-awareness alerts (SDIs),
                 based on application date in CA/CAplus and USPATFULL/USPAT2
                 may be affected by a change in filing date for U.S.
                 applications.
                 Improved searching of U.S. Patent Classifications for
NEWS 18 APR 28
                 U.S. patent records in CA/CAplus
                 GBFULL enhanced with patent drawing images
NEWS 19 MAY 23
                 REGISTRY has been enhanced with source information from
NEWS 20 MAY 23
                 CHEMCATS
NEWS 21 MAY 26
                 STN User Update to be held June 6 and June 7 at the SLA 2005
                 Annual Conference
NEWS EXPRESS
             JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
              STN Operating Hours Plus Help Desk Availability
NEWS HOURS
              General Internet Information
NEWS INTER
              Welcome Banner and News Items
NEWS LOGIN
NEWS PHONE
              Direct Dial and Telecommunication Network Access to STN
NEWS WWW
              CAS World Wide Web Site (general information)
Enter NEWS followed by the item number or name to see news on that
```

All use of STN is subject to the provisions of the STN Customer

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 17:19:04 ON 03 JUN 2005

=> file reg
COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 17:19:14 ON 03 JUN 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 JUN 2005 HIGHEST RN 851586-61-3 DICTIONARY FILE UPDATES: 2 JUN 2005 HIGHEST RN 851586-61-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=>

Uploading C:\Program Files\Stnexp\Queries\10088852.str

```
chain nodes :
11 19 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17
chain bonds :
7-11 11-12 19-20 20-21 21-22
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
exact/norm bonds :
7-11 11-12 21-22
exact bonds :
19-20 20-21
normalized bonds :
1-2 \quad 1-6 \quad 2-3 \quad 2-7 \quad 3-4 \quad 3-10 \quad 4-5 \quad 5-6 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17
```

G1:0,S,N,SO2

Hydrogen count :
9:= exact 1
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:A

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

# L1 STRUCTURE UPLOADED

=> d 11 L1 HAS NO ANSWERS L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 11 ful

FULL SEARCH INITIATED 17:19:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 23311 TO ITERATE

100.0% PROCESSED 23311 ITERATIONS

76 ANSWERS

SEARCH TIME: 00.00.01

L2 76 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 161.33 161.54

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 17:19:45 ON 03 JUN 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 3 Jun 2005 VOL 142 ISS 24 FILE LAST UPDATED: 2 Jun 2005 (20050602/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12 L3 4 L2

=> d 13 1- ibib abs hitstr YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:120821 CAPLUS

DOCUMENT NUMBER:

140:163886

TITLE:

Preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases

INVENTOR(S): Gazit, Aviv; Levitzki, Alexander

PATENT ASSIGNEE(S):

Yissum Research Development Company of the Hebrew

University of Jerusalem, Israel

SOURCE:

PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

OTHER SOURCE(S):

GI

| PAT  | ENT                          | NO. |     |     | KIN      | D   | DATE         |     |                        | APPL:         | ICAT: | DATE |     |     |     |     |          |  |  |  |
|------|------------------------------|-----|-----|-----|----------|-----|--------------|-----|------------------------|---------------|-------|------|-----|-----|-----|-----|----------|--|--|--|
|      | <br>2004013091<br>2004013091 |     |     |     | A2<br>A3 |     | 2004<br>2004 |     | Ţ                      | WO 2003-IL632 |       |      |     |     |     |     | 20030731 |  |  |  |
| "0   | W:                           | AE, | AG, | AL, | AM,      | AT, | AU,<br>DK,   | AZ, |                        | •             | •     | •    | •   | •   | •   | •   | •        |  |  |  |
|      |                              | GM, | HR, | HU, | ID,      | IL, | IN,          | IS, | JP,                    | KE,           | KG,   | KP,  | KR, | KZ, | LC, | LK, | LR,      |  |  |  |
|      |                              | •   | •   | •   | •        | •   | MD,<br>RU,   | •   |                        |               |       |      |     |     |     |     | -        |  |  |  |
|      | ₽₩•                          | •   | •   | •   | •        | •   | US,<br>MZ,   | •   | •                      | •             | •     | •    | •   |     | AM. | A7. | BY.      |  |  |  |
|      | 1000                         | KG, | KZ, | MD, | RU,      | ТJ, | TM,          | AT, | BE,                    | BG,           | CH,   | CY,  | CZ, | DE, | DK, | EE, | ES,      |  |  |  |
|      |                              |     |     |     |          |     | IE,<br>CM,   |     |                        |               |       |      |     | NE, | SŅ  | TD, | TG       |  |  |  |
| RITY | APP                          |     |     |     |          |     |              |     | US 2002-399736P P 2002 |               |       |      |     |     |     |     | 801 /    |  |  |  |

MARPAT 140:163886

 $(R^3)_n \xrightarrow{\text{II}}_{N} R^2$ 

ΙI

AB Title compds. I [R1 = (un) substituted Ph, naphthyl, etc.; R2 = H, halo, phenylamino, etc.; R3 = H, alkoxy, NO2, etc.; n = 1-3] are prepared For instance, 4-chloro-6-methylquinazoline is reacted with 2-aminophenol (EtOH, reflux, 1 h) to give II. I are potent inhibitors of protein tyrosine (PTK) kinase activity, particularly epidermal growth factor receptor (EGFR) kinase activity. I are useful in treating a variety of PTK related disorders such as cell proliferative disorders, fibrotic disorders, metabolic disorders and cancer.

IT 655248-61-6P, 3-[2-Bromo-4-((6,7-dimethoxyquinazoline-4-yl)amino)phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]acrylamide 655248-62-7P, N-Benzyl-3-[2-bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyanoacrylamide 655248-63-8P, 3-[2-Bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyano-N-(4-yl)amino-N-(4-yl)am

ale

CN

phenylbutyl)acrylamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

RN 655248-61-6 CAPLUS

2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 655248-62-7 CAPLUS

2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 655248-63-8 CAPLUS

CN 2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-(4-phenylbutyl)- (9CI) (CA INDEX NAME)

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228866 CAPLUS

DOCUMENT NUMBER: 134:266317

Preparation of quinazolines as aurora 2 kinase TITLE:

inhibitors

Mortlock, Andrew Austen; Keen, Nicholas John; Jung, INVENTOR(S):

Frederic Henri; Brewster, Andrew George Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 306 pp.

CODEN: PIXXD2

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PAT                  | ENT 1   | 10.   |     |     | KIND DATE   |     |     |                 |                |      | LICAT |          | DATE     |     |          |      |     |  |
|----------------------|---------|-------|-----|-----|-------------|-----|-----|-----------------|----------------|------|-------|----------|----------|-----|----------|------|-----|--|
| WO                   | 20010   | 02159 | 96  |     | A1 20010329 |     |     |                 |                |      |       | 20000918 |          |     |          |      |     |  |
|                      | W:      | AE,   | AG, | AL, | AM,         | AT, | AU, | AZ,             | BA,            | ВВ   | , BG, | BR,      | BY,      | BZ, | CA,      | CH,  | CN, |  |
|                      |         | CR,   | CU, | CZ, | DE,         | DK, | DM, | DZ,             | EE,            | ES   | , FI, | GB,      | GD,      | GE, | GH,      | GM,  | HR, |  |
|                      |         | HU,   | ID, | IL, | IN,         | IS, | JP, | KE,             | KG,            | KP   | KR,   | KZ,      | LC,      | LK, | LR,      | LS,  | LT, |  |
|                      |         |       | -   | -   |             |     |     |                 |                |      | , MZ, |          |          |     |          |      |     |  |
|                      | SD, SE, |       | -   |     |             |     |     |                 |                |      |       |          |          |     |          |      |     |  |
|                      | YU, ZA, |       | •   | •   | •           | •   | -   | -               |                |      |       |          | •        | ·   | •        | ·    |     |  |
|                      | RW:     |       | ,   | •   | •           | •   | •   | •               | •              |      | , TZ, |          |          | AT, | BE,      | CH,  | CY, |  |
|                      |         | •     | •   | •   | •           |     |     | •               |                |      | , LU, |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 |                |      | , NE, |          |          |     | •        | -    | •   |  |
|                      |         |       |     |     |             |     |     | CA 2000-2384291 |                |      |       |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 | BR 2000-14116  |      |       |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 |                |      |       |          | 20000918 |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 |                |      | , IT, |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     | MK,             |                |      |       | •        | ,        | •   | •        | •    | •   |  |
| JР                   | 2003    |       |     |     |             |     |     |                 | JP 2001-524975 |      |       |          |          |     | 20000918 |      |     |  |
|                      |         |       |     |     |             |     |     |                 | EE 2002-119    |      |       |          |          |     |          |      |     |  |
|                      | 1064    |       |     |     |             |     |     |                 | BG 2002-106492 |      |       |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 | ZA 2002-2234   |      |       |          |          |     |          |      |     |  |
|                      |         |       |     |     |             |     |     |                 | NO 2002-1399   |      |       |          |          |     |          |      |     |  |
| IORITY APPLN. INFO.: |         |       |     |     |             |     |     |                 |                |      | 1999- |          |          |     |          | 9990 | 921 |  |
| <br>                 |         |       |     |     |             |     |     |                 |                |      | 1999- |          |          |     |          | 9990 |     |  |
|                      |         |       |     |     |             |     |     |                 |                | WO : | 2000- | GB35     | 80       | ,   | w 2      | 0000 | 918 |  |

MARPAT 134:266317 OTHER SOURCE(S):

GI

$$R^{1}$$
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{6}$ 
 $R^{7}$ 
 $R^{7}$ 
 $R^{7}$ 
 $R^{8}$ 
 $R^{8}$ 
 $R^{8}$ 
 $R^{6}$ 
 $R^{6}$ 

Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR12; R12 = H or AB alkyl; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R13, or R15X1; R13 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, CO2, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R15 = H or (un) substituted hydrocarbyl, heterocyclyl, or alkoxy; R5 = NHCO2R9, NHCOR9, NHSO2R9, COR9, CO2R9, SOR9, SO2OR9, CONR10R11, SONR10R11, or SO2NR10R11; R9-R11 = independently H or (un) substituted hydrocarbyl or heterocyclyl; or R10 and R11 together with the N to which they are attached = (un) substituted heterocyclyl; R6 = H or (un) substituted hydrocarbyl or heterocyclyl; R7 and R8 = independently H, halo, alkyl, (di)alkoxy(methyl), alkanoyl, CF3, CN, NHY2, alkenyl, alkynyl, or (un) substituted Ph, PhCH2, or heterocyclyl; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, a 7-step sequence involving (1) alkylation of morpholine with 1-bromo-3-chloropropane (49%), (2) addition of Et vanillate to yield Et 3-methoxy-4-(3morpholinopropoxy)benzoate (100%), (3) nitration (86%), (4) reduction to the amine using 10% Pd/C (100%), (5) cycloaddn. with formamide to form the quinazoline(68%), (6) chlorination to give 4-chloro-6-methoxy-7-(3morpholinopropoxy) quinazoline (60%), and (7) amination with N-benzoyl-4-aminoaniline (58%) yielded II. The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration

II

0.0193  $\mu$ M. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.06  $\mu$ M and reduced BrdU incorporation into cellular DNA by 50% at 0.159-0.209  $\mu$ M.

### IT 331776-88-6P

of

RN

CN

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 4-substituted quinazoline aurora 2 kinase inhibitors for treatment of cancer and other proliferative diseases) 331776-88-6 CAPLUS

2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

2001:228865 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:266316

TITLE: Preparation of quinazoline derivatives, method of

preparation and use in inhibiting aurora 2 kinase

Mortlock, Andrew Austen; Keen, Nicholas John INVENTOR(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| F      | PATENT NO.            |       |             |             |     |             |            | DATE            |                | APPLICATION NO. |   |       |       |          |          | DATE     |      |     |  |  |
|--------|-----------------------|-------|-------------|-------------|-----|-------------|------------|-----------------|----------------|-----------------|---|-------|-------|----------|----------|----------|------|-----|--|--|
| -<br>V |                       |       |             | A1 20010329 |     |             |            |                 |                |                 |   | 2     | 0000  | 918      |          |          |      |     |  |  |
|        |                       | W:    | ΑE,         | AG,         | AL, | AM,         | ΑT,        | ΑU,             | ΑZ,            | BA,             | BB  | , BG, | BR,   | BY,      | ΒZ,      | CA,      | CH,  | CN, |  |  |
|        |                       |       | CR,         | CU,         | CZ, | DE,         | DK,        | DM,             | DZ,            | EE,             | ES  | , FI, | GB,   | GD,      | GE,      | GH,      | GM,  | HR, |  |  |
|        |                       |       | HU,         | ID,         | IL, | IN,         | IS,        | JP,             | KE,            | KG,             | KP  | , KR, | KZ,   | LC,      | LK,      | LR,      | LS,  | LT, |  |  |
|        |                       |       |             |             |     |             |            |                 |                |                 |   | , MZ, |       |          |          |          |      |     |  |  |
|        |                       |       | SD,         | SE,         | SG, | SI,         | SK,        | SL,             | ТJ,            | TM,             | TR  | TT,   | TZ,   | UA,      | ŪG,      | US,      | UΖ,  | VN, |  |  |
|        |                       |       | YU,         | ZA,         | ZW, | AM,         | AZ,        | BY,             | KG,            | KZ,             | MD  | , RU, | ТJ,   | TM       |          |          |      |     |  |  |
|        |                       | RW:   | GH,         | GM,         | KE, | LS,         | MW,        | MZ,             | SD,            | SL,             | SZ  | , TZ, | ŬĠ,   | ZW,      | ΑT,      | BE,      | CH,  | CY, |  |  |
|        |                       |       | DE,         | DK,         | ES, | FI,         | FR,        | GB,             | GR,            | ΙE,             | IT  | , LU, | MC,   | NL,      | PT,      | SE,      | BF,  | ВJ, |  |  |
|        |                       |       | CF,         | CG,         | CI, | CM,         | GΑ,        | GN,             | GW,            | ML,             | MR  | , NE, | SN,   | TD,      | TG       |          |      |     |  |  |
| (      | CA                    | 23842 |             | AA 20010329 |     |             |            | CA 2000-2384284 |                |                 |   |       |       | 20000918 |          |          |      |     |  |  |
|        |                       |       |             |             |     | A 20020521  |            |                 |                |                 |   |       |       |          | 20000918 |          |      |     |  |  |
| F      | ΞP                    | 1218  | 357         |             |     | A1 20020703 |            |                 |                | EΡ              | 2000-   | 9626  |       | 20000918 |          |          |      |     |  |  |
| F      | ΞΡ                    | 1218  | B1 20050406 |             |     |             |            |                 |                |                 | 20000918<br>20000918<br>20000918<br>SE, MC, PT, |       |       |          |          |          |      |     |  |  |
|        |                       | R:    | AT,         | BE,         | CH, | DE,         | DK,        | ES,             | FR,            | GB,             | GR  | , IT, | LI,   | LU,      | NL,      | SE,      | MC,  | PT, |  |  |
|        |                       |       | IE,         | SI,         | LT, | LV,         | FI,        | RO,             | MK,            | CY,             | AL  | ı     |       |          |          |          |      |     |  |  |
| j      | JP                    | 2003  | 5094        | 98          |     | Т2          | 2003       | 0311            | JP 2001-524974 |                 |   |       |       |          | 20000918 |          |      |     |  |  |
| F      | EΕ                    | 2002  | 0014        | 8           |     | Α           |            |                 | EE 2002-148    |                 |   |       |       |          |          |          |      |     |  |  |
| _      |                       | 2926  | 28          |             |     | E           | 2005       | 0415            | AT 2000-962682 |                 |   |       |       |          | 20000918 |          |      |     |  |  |
| 2      | ZA                    | 2002  | 0018        | 31          |     | A 20030605  |            |                 | ZA 2002-1831   |                 |   |       |       |          | 20020305 |          |      |     |  |  |
| N      | NO 2002001395         |       |             |             |     |             | A 20020515 |                 |                | NO 2002-1395    |   |       |       |          |          | 20020320 |      |     |  |  |
| F      |                       |       |             |             |     |             |            |                 |                | BG 2002-106535  |   |       |       |          |          |          |      |     |  |  |
| PRIOR  | RIORITY APPLN. INFO.: |       |             |             |     |             |            |                 |                |                 |   | 1999- |       |          |          |          |      |     |  |  |
|        |                       |       |             |             |     |             |            |                 |                |                 | WO  | 2000- | -GB35 | 62       |          | W 2      | 0000 | 918 |  |  |
| OTHER  | THER SOURCE(S):       |       |             |             |     |             | PAT        | 134:            | 2663           | 16              |   |       |       |          |          |          |      |     |  |  |
| GI     |                       |       |             |             |     |             |            |                 |                |                 |   |       |       |          |          |          |      |     |  |  |

## \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

I or a salt, ester, amide or prodrug thereof, a method for the preparation of I and the use of the claimed compds. for inhibiting aurora 2 kinase are claimed. These compds. are useful in the treatment of cancer. In I: X is O, or S, S(O) or S(O)2 or NR10 where R10 is H or C1-6 alkyl. R5 is OR11, NR12R13 or SR11 where R11, R12 and R13 are independently optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R12 and R13 may addnl. form together with the N atom to which they are attached, an optionally substituted aromatic or nonarom. heterocyclic ring which may contain further heteroatoms. R6 and R7 are independently H or hydrocarbyl. R8 and R9 are independently H, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkoxymethyl, di(C1-4alkoxy)methyl, C1-4 alkanoyl, trifluoromethyl, cyano, amino, C2-5 alkenyl, C2-5 alkynyl, a Ph group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms,

selected independently from O, S and N, which heterocyclic group may be aromatic or nonarom. and may be saturated (linked via a ring C or N atom) or unsatd. (linked via a ring C atom), and which Ph, benzyl or heterocyclic group may bear on one or more ring C atoms up to 5 substituents selected from hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C2-4 alkanoyl, C1-4 alkanoylamino, C1-4 alkoxycarbonyl, C1-4 alkylthio, C1-4 alkylsulfinyl, C1-4 alkylsulfonyl, carbamoyl, N-C1-4alkylcarbamoyl, N,N-di(C1-4alkyl) carbamoyl, aminosulfonyl, N-C1-4alkylaminosulfonyl, N,N-di(C1-4alkyl)aminosulfonyl, C1-4 alkylsulfonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C1-4alkoxycarbonyl. R1, R2, R3, R4 are independently halo, cyano, nitro, C1-3 alkylthio, -N(OH)R14 (R14 is H, or C1-3 alkyl), or R16X1- (X1 represents a direct bond, -0-, -CH2-, -OC(0)-, -C(O)-, -S-, -SO-, -SO2-, -NR17C(O)-, -C(O)NR18-, -SO2NR19-, -NR20SO2- or -NR21- (R17, R18, R19, R20 and R21 each independently represents H, C1-3 alkyl or C1-3alkoxyC2-3alkyl), and R16 is H, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy). A method for preparing I comprises reacting II where X, R8 and R9 are as defined above, R1', R2', R3', R4' are groups R1, R2, R3, R4 as defined above resp., or precursors thereof; and R85 is a leaving group, with HCR6:CR7C(0)R5', where R6 and R7 are as defined above, R5' is a group R5 as defined above or a precursor group therefore; and thereafter if desired or necessary, converting any precursor groups R1', R2', R3', R4' or R5' to groups R1, R2, R3, R4 or R5 resp., or changing a group R5 to a different such group. The compds. of the invention inhibit the serine/threonine kinase activity of the aurora 2 kinase and thus inhibit the cell cycle and cell proliferation. Procedures for assessing these properties are described and test results are given for (E)-4-[4-(2-(3-methylcyclohexylaminocarbonyl)ethenyl)anilino]-6,7dimethoxyquinazoline.

IT 331734-29-3P, (E)-4-[4-(2-Carboxyethenyl)anilino]-6,7dimethoxyquinazoline 331734-31-7P, (E)-4-[4-(2Carboxyethenyl)anilino]-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline
hydrochloride

Die DCT (Boogtopt): SDN (Symthotic proparation): PDEP (Preparation): PAC

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of quinazoline derivs., method of preparation and use

in inhibiting aurora 2 kinase)

RN 331734-29-3 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-31-7 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, hydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

#### ●x HCl

#### IT 331733-89-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of quinazoline derivs., method of preparation and use in inhibiting

aurora 2 kinase)

RN 331733-89-2 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 331733-38-1P 331733-40-5P 331733-41-6P 331733-43-8P 331733-44-9P 331733-46-1P 331733-48-3P 331733-50-7P 331733-52-9P 331733-53-0P 331733-55-2P 331733-57-4P 331733-69-6P 331733-61-0P 331733-64-3P 331733-77-8P 331733-79-0P 331733-80-3P

```
331733-81-4P 331733-82-5P 331733-83-6P
    331733-84-7P 331733-85-8P 331733-86-9P
    331733-87-0P 331733-88-1P 331733-90-5P
    331733-91-6P 331733-92-7P 331733-93-8P
    331733-94-9P 331733-95-0P 331733-96-1P
    331733-97-2P 331733-98-3P 331733-99-4P
    331734-00-0P 331734-01-1P 331734-02-2P
    331734-03-3P 331734-04-4P 331734-05-5P
    331734-06-6P 331734-07-7P 331734-08-8P
    331734-09-9P 331734-10-2P 331734-11-3P
    331734-12-4P 331734-13-5P 331734-14-6P
    331734-15-7P 331734-16-8P 331734-17-9P
    331734-19-1P 331734-20-4P 331734-21-5P
    331734-22-6P 331734-23-7P 331734-24-8P
    331734-25-9P 331734-26-0P 331734-27-1P,
     (E)-4-[4-(2-Carboethoxyethenyl)anilino]-6,7-dimethoxyquinazoline
    331734-28-2P, (E)-4-[4-(2-Carboethoxyethenyl)phenoxy]-6,7-
    dimethoxyquinazoline
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of quinazoline derivs., method of preparation and use in
inhibiting
       aurora 2 kinase)
RN
     331733-38-1 CAPLUS
     2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-phenyl-
     , (2E) - (9CI) (CA INDEX NAME)
```

Double bond geometry as shown.

RN 331733-40-5 CAPLUS
CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-ethyl-,
(2E)- (9CI) (CA INDEX NAME)

RN 331733-41-6 CAPLUS

CN Morpholine, 4-[(2E)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-1-oxo-2-propenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-43-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(4-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-44-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(1,3-dimethylbutyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c} \text{MeO} \\ \text{MeO} \\ \\ \text{HN} \\ \\ \text{O} \end{array} \begin{array}{c} \text{H} \\ \text{Bu-i} \\ \\ \text{O} \end{array}$$

RN 331733-46-1 CAPLUS

CN 2-Propenamide, N-[(2-chlorophenyl)methyl]-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-48-3 CAPLUS

CN 2-Propenamide, N-(2,3-dihydroxypropyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-50-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylpropyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-52-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-53-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxyethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-55-2 CAPLUS

CN 2-Propenamide, N-(cyanomethyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-57-4 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-[3-(dimethylamino)propyl]-, (2E)- (9CI) (CA INDEX NAME)

MeO 
$$\frac{N}{N}$$
  $\frac{E}{N}$   $\frac{H}{N}$   $\frac{NMe_2}{N}$ 

CN 2-Propenamide, N-butyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-61-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxy-1-methylethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-64-3 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-68-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methylcyclohexyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-71-2 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-75-6 CAPLUS

CN 2-Propenamide, N-(4-chlorotetrahydro-1,1-dioxido-3-thienyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-77-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-[(5-methyl-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-79-0 CAPLUS

CN 2-Propenamide, N-cyclopropyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-80-3 CAPLUS

CN 2-Propenamide, N-cyclobutyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-81-4 CAPLUS

CN 2-Propenamide, N-cyclopentyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-82-5 CAPLUS
CN 2-Propenamide, N-cyclohexyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-83-6 CAPLUS

CN Piperidine, 1-[(2E)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-1-oxo-2-propenyl]- (9CI) (CA INDEX NAME)

RN 331733-84-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-85-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-86-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-87-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-88-1 CAPLUS

CN 2-Propenamide, N-(4-chlorophenyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-90-5 CAPLUS

CN 2-Propenamide, N-(cyclohexylmethyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$O$$

RN 331733-91-6 CAPLUS

CN 2-Propenamide, N-(6-chloro-3-pyridinyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-92-7 CAPLUS

CN 2-Propenamide, N-(2-furanylmethyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$O$$

$$O$$

RN 331733-93-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[(tetrahydro-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$O$$

RN 331733-94-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-2-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-95-0 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-96-1 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-97-2 CAPLUS
CN 2-Propenamide, N-(1,3-dimethylbutyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX

Double bond geometry as shown.

NAME)

RN 331733-98-3 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2,2,2-trifluoroethyl)-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$
 $(CH_2)_3$ 
 $(CH_2)_3$ 

RN 331733-99-4 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylpropyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-00-0 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$N$$

$$Pr-n$$

RN 331734-01-1 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-02-2 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$HN$$

RN 331734-03-3 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[2-(2-thienyl)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-04-4 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[(5-methyl-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

PAGE 1-A

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$O$$

$$O$$

PAGE 1-B

<sup>─</sup>Me

RN 331734-05-5 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(tetrahydro-1,1-dioxido-3-thienyl)-, (2E)-(9CI) (CA INDEX NAME)

$$(CH_2)_3$$
 $(CH_2)_3$ 
 $(CH_2)_3$ 

RN 331734-06-6 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[2-(methylthio)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$(CH_2)_3 \xrightarrow{O} \qquad N$$

$$MeO \qquad \qquad HN$$

$$E \qquad \qquad H$$

$$O \qquad SMe$$

RN 331734-07-7 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

RN 331734-08-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[2-(methylthio)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-09-9 CAPLUS

CN 2-Propenamide, N-cyclopentyl-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-10-2 CAPLUS

CN 2-Propenamide, N-cyclohexyl-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-11-3 CAPLUS

CN 2-Propenamide, N-(cyclohexylmethyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-12-4 CAPLUS

CN 2-Propenamide, N-(6-chloro-3-pyridinyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-13-5 CAPLUS

CN 2-Propenamide, N-(2-furanylmethyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-14-6 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[(tetrahydro-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-15-7 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-16-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-17-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2,2,2-trifluoroethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-19-1 CAPLUS

CN 2-Propenamide, N-(2,3-dihydroxypropyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-20-4 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-21-5 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(3-methylcyclohexyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-22-6 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-23-7 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[2-(2-thienyl)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-24-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(tetrahydro-1,1-dioxido-3-thienyl)-, (2E)-(9CI) (CA INDEX NAME)

RN 331734-25-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(phenylmethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-26-0 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-27-1 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

RN 331734-28-2 CAPLUS
CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228864 CAPLUS

DOCUMENT NUMBER: 134:252355

TITLE: Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

|      |                       |            |     |     |     |     | KIND        |      | DATE                          |                   | APPLICATION NO. |        |       |     |          |          | DATE  |     |  |
|------|-----------------------|------------|-----|-----|-----|-----|-------------|------|-------------------------------|-------------------|-----------------|--------|-------|-----|----------|----------|-------|-----|--|
|      | WO                    | 2001       | 94  |     |     |     |             |      | WO 2000-GB3556                |                   |                 |        |       |     | 20000918 |          |       |     |  |
|      |                       | W:         | ΑE, | AG, | AL, | AM, | AT,         | ΑU,  | ΑZ,                           | BA,               | BE              | , BG,  | BR,   | BY, | ΒZ,      | CA,      | CH,   | CN, |  |
|      |                       |            | CR, | CU, | CZ, | DE, | DK,         | DM,  | DZ,                           | EE,               | ES              | FI,    | GB,   | GD, | GE,      | GH,      | GM,   | HR, |  |
|      |                       |            | HU, | ID, | IL, | IN, | IS,         | JP,  | ΚE,                           | KG,               | KE              | , KR,  | ΚZ,   | LC, | LK,      | LR,      | LS,   | LT, |  |
|      |                       |            | LU, | LV, | MA, | MD, | MG,         | MK,  | MN,                           | MW,               | MX              | , MZ,  | NO,   | ΝZ, | PL,      | PT,      | RO,   | RU, |  |
|      |                       |            | SD, | SE, | SG, | SI, | SK,         | SL,  | ТJ,                           | TM,               | TF              | R, TT, | TZ,   | UA, | UG,      | US,      | UΖ,   | VN, |  |
|      |                       |            | YU, | ZA, | ZW, | AM, | ΑZ,         | BY,  | KG,                           | ΚZ,               | MI              | , RU,  | ТJ,   | TM  |          |          |       |     |  |
|      |                       | RW:        | GH, | GM, | ΚE, | LS, | MW,         | MZ,  | SD,                           | SL,               | SZ              | , TZ,  | ŬG,   | ZW, | ΑT,      | BE,      | CH,   | CY, |  |
|      |                       |            |     |     |     |     |             |      |                               |                   |                 | LU,    |       |     |          | SE,      | BF,   | ΒJ, |  |
|      |                       |            | CF, | CG, | CI, | CM, | GΑ,         | GN,  | GW,                           | ML,               | MF              | R, NE, | SN,   | TD, | ΤG       |          |       |     |  |
|      |                       | A 2384282  |     |     |     |     |             |      |                               | CA 2000-2384282   |                 |        |       |     |          |          |       |     |  |
|      |                       | 2000014133 |     |     |     |     |             |      |                               | BR 2000-14133     |                 |        |       |     |          |          |       |     |  |
|      | TR                    | 200200749  |     |     |     | Т2  | T2 20020621 |      |                               | TR 2002-200200749 |                 |        |       |     |          | 20000918 |       |     |  |
|      | EΡ                    |            |     |     |     |     |             |      | EP 2000-962677                |                   |                 |        |       |     |          |          |       |     |  |
|      |                       | R:         |     |     |     |     |             |      |                               |                   |                 | R, IT, | LI,   | LU, | ΝL,      | SE,      | MC,   | PT, |  |
|      |                       |            |     |     |     |     |             | RO,  | MK,                           | CY,               | ΑI              | ٠      |       |     |          |          |       |     |  |
|      | JP 2003509497         |            |     |     |     |     |             |      | JP 2001-524973<br>EE 2002-149 |                   |                 |        |       |     | 20000918 |          |       |     |  |
|      | EE 200200149          |            |     |     |     |     | 2003        | 0415 |                               | EΕ                | 2002-           | -149   |       |     | 2        |          |       |     |  |
|      | AU 763242             |            |     |     |     |     |             |      |                               |                   | 2000-           |        |       |     |          | 0000     |       |     |  |
|      | ZA 2002001833         |            |     |     |     | Α   |             |      |                               |                   |                 |        |       |     |          |          | 0020  |     |  |
|      | BG 106491             |            |     |     |     | Α   |             |      |                               |                   |                 | 2002-  |       |     |          | _        | 0020  |     |  |
|      | NO 2002001401         |            |     |     |     | Α   |             | 2002 | 0521                          |                   |                 | 2002-  |       |     |          |          | 0020  |     |  |
| PRIO | RIORITY APPLN. INFO.: |            |     |     |     |     |             |      |                               |                   |                 | 1999-  |       |     |          |          |       |     |  |
|      |                       |            |     |     |     |     |             |      |                               |                   |                 | 1999-  |       |     |          |          |       |     |  |
|      |                       |            |     |     |     |     |             |      |                               |                   |                 | 1999-  |       | -   |          |          | .9990 | -   |  |
|      |                       |            |     |     |     |     |             | 104  |                               |                   | WO              | 2000-  | -GB35 | 56  |          | W 2      | 20000 | 918 |  |

OTHER SOURCE(S): MARPAT 134:252355

GI

$$R^2$$
 $R^3$ 
 $R^4$ 
 $R^3$ 
 $R^4$ 
 $R^4$ 
 $R^3$ 

AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; Ra = (un)substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 4-phenoxyaniline•HCl and 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.069 μM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 2.89 μM and reduced BrdU incorporation into cellular DNA by 50% at 3.68 μM.

II

## IT 330999-73-0

RN

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; preparation of 4-substituted quinazoline aurora 2 kinase
 inhibitors for treatment of cancer and other proliferative diseases)
330999-73-0 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT